daily amphotericin (31%). Fungal prophylaxis was started pre-transplant at 85% of the institutions, day +1 (15%) of the institutions. Fungal prophylaxis was stopped with immunosuppressive therapy at 69% of the centers, day +21 (7%), day +100 (7%) and 17% of reporting institutions did not specify. Ninety-three percent of the institutions used prophylaxis for cGVHD patients.

Fifty-percent routinely screen for fungal infections after day 0 in both autologous and allogeneic transplants, utilizing weekly culture surveillance (23%), fever only (25%), fever/clinical evidence (45%) and by Glactamann assay (7%). Fungal organisms screened for included Canididia (53%), Histoplasma (31%), Crytpotococcus (15%), Aspergillus (85%), Zygomyces (45%) and Fusarium (31%).

The majority reported using hepa-filtered rooms and hand washing. N-95 masks (31%) were part of BMT isolation policy and 11% used gowns. There were age specific visitor restrictions at 50% of the institutions with no visitors under an age range of 12 to15 years old.

Based on the submitted surveys the PBMTC institutions employ various fungal management practices. These findings suggest a need to develop a fungal management standard of care for the pediatric BMT patient. Further exploration of practices and outcomes is needed to expand evidence based fungal management practices in the pediatric BMT patient.

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RESOLUTION OF IPEX AND ACHIEVEMENT OF COMPLETE DONOR CD3$^+$CD4$^+$ T-CELL ENGRAFTMENT FOLLOWING A REDUCED INTENSITY CONDITIONING REGIMEN AND INFUSION OF A T- AND B-LYMPHOCYTE DEPLETED ALLOGENEIC BONE MARROW GRAFT

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Immune dysregulation, polyendocrinopathy, enteropathy, X-linked syndrome (IPEX) is a rare autoimmune disease, historically resulting in death by 2 years of age. IPEX is characterized by mutations in FOXP3, resulting in aberrant function of CD4$^+$CD25^{bright} regulatory T cells (Treg). Treg are critical regulators of immune responses and dysfunctional activity results in unchecked immune-mediated disease. Allogeneic hematopoietic stem cell transplantation (HSCT) is the only potential cure, yet traditional myeloablative conditioning, tends to be detrimental to this population. Our patient, who has a FOXP3 missense mutation at 1150 G>A, presented with severe enteropathy, failure to thrive, psoriasiform dermatitis, and sepsis in early infancy. Prior to HSCT at 8 months of age, he developed autoimmune hemolytic anemia while receiving immunosuppressive therapy. For HSCT, he received a reduced intensity conditioning (RIC) regimen consisting of Campath-1H, fludarabine, thiotepa, and melphalan, followed by a T- and B-cell depleted matched unrelated donor bone marrow graft with 5×10^6 CD3$^+$ cells/kg added back to facilitate engraftment. Cyclosporine was continued for graft-versus-host disease prophylaxis. Due to his severe enteropathy he received palifermin 3 days prior to beginning RIC and 3 days after HSCT. Conditioning and stem cell infusion were well tolerated. The patient achieved myeloid engraftment (ANC > 500/mm^3) on day +13 and platelet engraftment (>50,000/mm^3) on day +37. He reveals no clinical signs of IPEX, including resolution of enteropathy and reduction in serum IgE from 299 International units (IU)/ml to 4 IU/ml at day +27; this marker remains within normal limits. Initial peripheral blood chimerism by VNTR analysis was 100%, yet decreased over time, leading to the discontinuation of cyclosporine on day +91. To determine presence of Treg, myeloid and lymphocyte subsets were purified by cell-sorting and analyzed by VNTR when cell populations were > 10,000 cells. Well-defined CD3$^+$CD4$^+$ and CD3$^+$CD8$^+$ T-cell populations were > 89% donor, with the Treg population being 98% donor. Myeloid and NK cells and B lymphocytes exhibit mixed chimerism 5 months after HSCT. Lymphocyte responses to mitogens were normal at day +152. In summary, we have demonstrated that a child with IPEX can tolerate HSCT with a RIC regimen and a T- and B-cell depleted graft with minimal toxicity and achieve full Treg lymphocyte engraftment in the presence of a mixed donor chimerism.

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TWICE-DAILY INTRAVENOUS (IV) BUSULFAN (Bu) X 4 DAYS IN CHILDREN UNDERGOING A REDUCED-INTENSITY CONDITIONING (RIC) REGIMEN WITH ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION (AlloHSCT) IS SAFE AND WELL-TOLERATED BUT RESULTS IN SIGNIFICANTLY INCREASED Bu CLEARANCE (CL) AND DECREASED AREA UNDER THE CURVE (AUC) AND HALF-LIFE ($t_{1/2}$) WHEN COMPARED TO IV BU TWICE-DAILY DOSING PHARMACOKINETICS (PK) IN ADULTS

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Inaccurate Bu dosing during HSCT conditioning can result in increased graft failure or excessive regimen-related toxicity. IV Bu is safe and effective in pediatric HSCT recipients at a dose of 4 mg/kg/day (≤4 yr) or 3.2 mg/kg/day (>4 yr) using q6 h × 16 dosing but Bu PK is age-dependent (Wall, Blood, 2000a). Q12 h × 8 dosing has been shown to be safe and effective in adults, with mean first-dose AUC 3576 mmol*min, $t_{1/2}$ 3.46 h and CL 1.88 ml/min/kg (Fernandez, BBMT, 2002). However, Bu safety and PK data is lacking for q12 h × 8 dosing in pediatric HSCT recipients. We studied 15 pediatric pts, mean age 9.5 yr (1.4–20.9 yr) with malignant (n = 5) and nonmalignant (n = 10) conditions who underwent RIC for alloHSCT with IV Bu q12 h × 8 dosing (4 mg/kg/day [< 4 yr]; 3.2 mg/kg/day [≥4 yr]), fludarabine (30 mg/m^2/day × 5 days) and alemtuzumab (54 mg/m^2/5 days). Phenytoin/fosphenytoin load was given prior to start of Bu; maintenance continued 48 h post-Bu. Donor sources were: 3 6/6 & 1 5/6 matched-related donor, 1 10/10, 2 9/10 & 2 8/10 MUD, 2 6/6 related cord blood (CB) and 4 4/6 unrelated CB. PK samples (n = 12) were obtained at hr 1, 2, 3, 5, 6, 7 and 8 after start of 1st dose. Bu levels were measured by a GC-MS method on heparinized plasma. Results are summarized in Table I. Target C_{ss} was 600–900 ng/ml. 5 pts required dose increases; 1 was dose-reduced. Mean CL (ml/min/kg) for <4 yr (n = 3) was significantly higher than in ≥4 yr (4.59 ± 0.52 v 3.45 ± 0.72, p = .0326). Difference between mean Bu $t_{1/2}$ for <4 yr v ≥4 yr trended toward but did not reach significance (1.94 h ± 0.46 v 2.57 h ± 0.59, p = 0.13). 2 pts (13%) had seizures unrelated to Bu; there was no VOD. Donor chimerism was 80% at D + 30 (n = 13) and 90% at D + 60 (n = 11). 1 of 15 pts had primary graft failure; this pt also had the 2nd highest Bu CL (4.77 ml/min/kg), lowest $t_{1/2}$ (1.62 h) and 2nd lowest AUC (1648 mmol*min). In summary, we demonstrated significantly lower AUC and $t_{1/2}$ and significantly increased CL when compared to adult q12h dosing PK data, suggesting that q12h IV Bu PK may depend on patient age (Table I). We also found a significant age-dependent (<4 yr v ≥4 yr) difference in Bu CL, possibly due to increased glutathione-S-transferase activity (Gibbs, Drug Metab Dispos, 1999). Furthermore, we showed that q12h IV Bu in pediatric pts results in low toxicity and high engraftment post-RIC regimen. Additional pediatric subjects are needed to determine if increased Bu CL and decreased AUC result in increased risk of graft failure.

Busulfan pharmacokinetic data for q12 hour dosing in pediatric and adult patients

	AUC mmol*min (mean ± SD)	$t_{1/2}$, hr (mean ± SD)	CL, ml/min/kg (mean ± SD)	Vd, L (mean ± SD)	C_{ss} ng/ml (mean ± SD)
Pediatric (n = 12; n = 11 for AUC & VD	1900 ± 383	2.41 ± 0.61	3.74 ± 0.83	22.8 ± 14.6	653 ± 125
Adult (n = 6) (Fernandez, BBMT, 2002)	3576 ± 740	3.46 ± 0.38	1.88 ± 0.37	Not Reported	Not Reported
p-value	p<.0001	p=.0015	p=.0001	NA	NA